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General Physiology is the study of biological mechanisms through analytical investigations, which decipher the molecular and cellular mechanisms underlying biological function at all levels of organization.

The mission of the *Journal of General Physiology* is to publish articles that elucidate important biological, chemical, or physical mechanisms of broad physiological significance.

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Cover picture: A mouse neuroblastoma (Neuro-2a) cell expressing α4-eGFPβ2 neuronal nicotinic acetylcholine receptors (nAChRs) was imaged using total internal reflection fluorescence (TIRF) microscopy (top left). The pseudo-colored TIRF image was processed to reveal either endoplasmic reticulum (middle) or plasma membrane (PM) fluorescence (right). The bar chart provides a pixel-by-pixel analysis of PM-integrated fluorescence density for α4-eGFPβ2 and α4-eGFPβ4 nAChRs (see article by Srinivasan et al., 59–79).

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Cover picture: Transfer of KcsA potassium channels from nanoscale apolipoprotein-bound bilayers (NABBs) to black lipid membranes. (Left) Schematic representation of KcsA incorporated into a discoidal lipoprotein particle and its subsequent insertion into a lipid bilayer. (Right) Single-channel current traces resulting from application of discs without channel (NABB), with small amounts of KcsA (1K-NABB), or large amounts of KcsA (4K-NABB; see article by Banerjee and Nimigean, 217–223).

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Cover picture: (Left) White skeletal muscle of adult zebrafish. Ultrastructure of chemically skinned muscle fibers. Relaxed myofibrils are surrounded by distended profiles of sarcoplasmic reticulum and Z-type triads only (arrows). (Right) Force transients of myofibrils isolated from adult zebrafish (dark gray) and from larvae (light gray) were induced by a fast solution change technique and recorded using atomic force microscopy (see article by Iorga et al., 255–270).

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Cover picture: (Top) Cartoons depicting translocation of lethal factor (LF) tagged with biotin (orange) through the anthrax toxin channel. (Bottom) Transbilayer currents in response to a series of voltage pulses (+80 mV for 5 s and −40 mV for 15 s) after LF is added to the *cis* side of the bilayer show unblocking of the channel in each cycle (blue line). The decrease of unblocking (red curve) after the addition of streptavidin to the *trans* side implies that the biotin residue at residue 1 of LF reaches the *trans* side of the channel (see article by Basilio et al., 343–356).

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Cover picture: Native sumoylation of Kv2.1 in rat hippocampal neurons shown by antibody-mediated FRET (left). Acceptor photobleaching of Alexa Fluor 488 on Kv2.1 (green) and Alexa Fluor 594 on SUMO2/3 reveals interaction at the cell surface (arrowhead), within (open arrow) and at the periphery of Kv2.1 clusters (solid arrow). Sumoylation shifts the conductance–voltage relationship up to 35 mV. Each channel tetramer carries no more than two SUMO1 monomers on lysine 470 of non-adjacent subunits (right); stoichiometry is determined by expression of Kv2.1 and GFP-tagged SUMO1 in CHO cells, TIRF visualization of the cell surface, and stepwise photobleaching (see article by Plant et al., 441–454).

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Cover picture: TRPA1 is activated by weak acids that acidify the cell cytosol. (Left) Changes in emission from the pH-sensitive fluorescent probe carboxy-DFFDA, reflecting intracellular acidification in HEK-293 cells in response to acetic acid at varying concentrations. (Right) A summary of data for a series of carboxylic acids of varied concentrations and pH. (Bottom) A model of how acetic acid and other weak acids activate TRPA1 (see article by Wang et al., 493–505).